**Institution: University of Glasgow**

**Unit of Assessment: B10 – Mathematical Sciences**

**Title of case study: Out of Africa**

## 1. Summary of the impact

Research in the School of Mathematics & Statistics in the University of Glasgow has been influential in answering a long-standing question: where do we come from? The fleshing-out of the ’out of Africa’ theory has been the focus of two documentary series, *The Incredible Human Journey* and *Meet the Izzards*, and has generated income for DNA testing companies in the UK and US by enabling them to offer ‘deep DNA’ tests revealing one’s roots from far back in history. *The Incredible Human Journey* aired on BBC 2 in 2009, reaching 10.2 million viewers altogether, has been watched 100,000 times on YouTube and was broadcast in shorter format in Australia and Canada before being released as a DVD. *Meet the Izzards* was broadcast on BBC 1 in 2013 to over 3 million people.

## 2. Underpinning research

The research provided the strongest genetic evidence to date of the route by which modern humans migrated out of east Africa some 60,000-80,000 years ago. This landmark study carried out by Dr Vincent Macaulay (Reader in Statistics, University of Glasgow, 2003-present) and an international team from 2003-2005 brought into radically sharper focus the ‘out of Africa’ theory of human dispersal. Prior to this it was generally believed that there was a series of dispersals from different areas of Africa, including a northerly wave which was ultimately to populate Europe. Macaulay et al.’s findings demonstrated that only one relatively small group of human ancestors travelled from Africa eventually to spread over the rest of the world; that this group travelled faster and further than previously believed; and that all humans outside Africa are ultimately descended from the same group of travellers.

Mitochondrial DNA (mtDNA) is passed down the maternal line, and is important to genetic archaeology because it is inherited intact (in contrast to most of our DNA) and has plenty of variation, generated when mutations occur between mother and child, which makes it possible to reconstruct the ancestry of the sequences in exquisite detail. If the mutation rate of mtDNA can be established, researchers can exploit that rate to convert genetic variation into time estimates to assign mutations to particular eras and places. Macaulay’s work focussed on developing statistical models to accomplish these two tasks from the complete mitochondrial DNA sequence data gathered from diverse living humans, in the context of international teams of human geneticists. He used techniques from graph theory (median networks) and likelihood approaches to help to reconstruct the ‘family tree’ of mtDNA [1]. His research then addressed spatial questions – what physical locations are associated with particular ancestors in this tree [2], before he turned to the temporal aspects, where it was vital better to model the clock which describes how rapidly particular genetic material changes by mutation. A technique for doing this was proposed [3] for the case where DNA is experiencing natural selection, so that in effect the clock appears to slow down as one moves into the past. This allowed a tool [3] to be developed to extract more temporal information from mtDNA sequences than was hitherto possible, so that the variation in mtDNA is much more securely anchored in time, a vital pre-requisite for robust genealogical interpretation at deep time depths.

Finally, and most challengingly, between 2003 and 2010 Macaulay modelled the *processes* that generated the inferred spatio-temporal signal in the tree. For example, these might involve migration, as in the high-profile study [2] which provides the strongest genetic evidence to date of the route by which modern humans migrated out of east Africa 60,000-80,000 years ago; by detecting temporal patterning in the distribution of inferred movements of ancestors in the tree ('founder analysis', the statistical properties of which have been explored [4] in the context of the structure coalescent process); or admixture, by dissecting the contribution of different regions of Africa to the Americas, as a result of the slave trade, by Bayesian modelling [5].

Macaulay has developed these approaches with three local research students in Statistics, Dr Noel Thomson (supported by a scholarship from the Carnegie Trust), Dr Maarya Sharif (supported by a studentship from EPSRC) and Dr Colette Mair (supported by a University of Glasgow scholarship). The University of Glasgow researchers have been solely responsible for developing the new statistical techniques and have shared the job of applying them, in various collaborative teams with wet-lab colleagues in other institutions in the UK and the rest of Europe (who focus on the sample collection, the DNA sequencing, and bioinformatics issues). The techniques have been most comprehensively applied to understanding genetic variation in human mitochondrial DNA, one of the main genetic loci that have been marketed by the genetic genealogical industry in the last 10 years. The specific University of Glasgow contribution to the impact was the statistical modelling that allowed inferences about time, place and process to be made from contemporary DNA sequences, inferences that have generated the impact in the genetic genealogy industry.

## 3. References to the research

1. Torroni, A., Achilli, A., Macaulay, V., Richards, M. and Bandelt, H.-J. (2006). Harvesting the fruit of the human mtDNA tree. *Trends in Genetics*, 22, 339-345. (doi:10.1016/j.tig.2006.04.001) *
2. Macaulay, V., Hill, C., Achilli, A., Rengo, C., Clarke, D., Meehan, W., Blackburn, J., Semino, O., Scozzari, R., Cruciani, F., Taha, A., Shaari, N. K., Raja, J. M., Ismail, P., Zainuddin, Z., Goodwin, W., Bulbeck, D., Bandelt, H.-J., Oppenheimer, S., Torroni, A. and Richards, M. (2005). Single, rapid coastal settlement of Asia revealed by analysis of complete mitochondrial genomes. *Science*, 308, 1034-1036 and 309, 1995-1996. (doi:10.1126/science.1109792) *
3. Soares, P., Ermini, L., Thomson, N., Mormina, M., Rito, T., Röhl, A., Salas, A., Oppenheimer, S., Macaulay, V. and Richards, M. B. (2009). Correcting for purifying selection: an improved human mitochondrial molecular clock. *American Journal of Human Genetics*, 84, 740-759. (doi:10.1016/j.ajhg.2009.05.001) *
4. Thomson, Noel (2010) Bayesian mixture modelling of migration by founder analysis. PhD thesis, University of Glasgow. (http://theses.gla.ac.uk/1468/)
5. Salas, A., Carracedo, Á., Richards, M., and Macaulay, V. (2005). Charting the ancestry of African-Americans. *American Journal of Human Genetics*, 77, 676-680. http://dx.doi.org/10.1086/491675

* best indicators of research quality

## 4. Details of the impact

The southern-route 'out of Africa' theory of human dispersal developed by University of Glasgow research has sparked huge ongoing public interest since its publication in 2005. The idea has been discussed in the TV series and popular science book *The Incredible Human Journey* by Alice Roberts in 2009/10. University of Glasgow research has also led to the creation of a revised timeline (based on a time-dependent molecular clock) for linking DNA changes with locations and times, which has been adopted by companies such as BritainsDNA, which offer DNA tests for people seeking information about their recent and deep ancestry. The 2013 TV programme *Meet the Izzards* is another high-profile show which used the Glasgow research in part to trace Eddie Izzard's ancestry back to the evolution of modern humans in east Africa.

*The Incredible Human Journey* was published by Bloomsbury in 2010. Roberts describes the 'out of Africa' theory in an accessible manner for a lay audience, and quotes the research papers by Macaulay et al. for those looking for more details. One reviewer on Amazon says, 'I am gripped by the central idea that only about 200 families originally emerged out of Africa and between them populated the whole world', one of the statistical inferences made by Macaulay.

The TV series was broadcast on BBC 2 from May-June 2009, as a 5-part series following the routes of the families who populated the world. The first part is titled 'Out of Africa' and gives a full picture of the earlier theories prior to the Macaulay et al paper in 2005, but each of the episodes recounts the general theory for viewers who had not seen the first one. The later episodes follow Macaulay et al.'s theory of the dispersal of humans across the planet. Over 10.2 million viewers watched the series when it was aired on the BBC, with Part 1, 'Out of Africa', being shown on 10 May and achieving an audience of 2.22m. Part 2, 'Asia', reached 2.34m; Part 3, 'Europe', was watched by 1.66m; Part 4, 'Australia' attracted 2.11m viewers; and Part 5, 'The Americas', reached an audience of 1.86m. The series is currently available to view on YouTube and the first episode has been viewed 101,562 times since it was added to the site in August 2011. It has also been widely reviewed as a series and book, with *The Observer* noting that it provides 'an easily digestible introduction to a complex but fascinating story.'

*Meet the Izzards* is a 2-part documentary, which aired on BBC 1 at a prime-time slot of 9pm on 20 and 21 February 2013, and was available on iPlayer. It was broadcast to an audience of 2.62 million (figures for Part 1 only). In the documentary, Izzard explains the 'out of Africa' concept to the audience: 'we all come out of Africa, and we come from the same people. So we were a small group of 10,000 people and then we've turned into seven billion people on the planet.' The programme received widespread press coverage. The consultant scientist acknowledges the programme's debt to Macaulay's work, stating that his mtDNA genealogy discoveries; *'…define a scientific framework for a number of documentaries, including Meet the Izzards but also other series which seek to educate the public and disseminate human population genetics to the lay public'.*

The consultant to the BBC programme is also Chief Scientific Officer (CSO) of BritainsDNA, one of a number of companies which have sprung up around the combination of DNA analysis and the public appetite for genealogy. BritainsDNA, established 2011 as ScotlandsDNA, draws upon the 'out of Africa' theory to analyse DNA samples from the public. This has tapped into the huge public interest in tracing their ancestors, allowing members of the public to trace their genetic lineage through DNA testing. BritainsDNA draws upon Macaulay et al.'s work to allocate dates and locations in history to the mtDNA samples taken from the public. The CSO for the company states:

> *Dr Macaulay's work underpins a significant part of the genetic ancestry testing business. Specifically his contributions to the understanding of the mtDNA genealogy – the topology or shape of the tree, the timing of many of the splits in the tree and the distribution of the groups across geography are the bread and butter of the interpretation of mtDNA lineages. This impact is felt not only at BritainsDNA but across all companies offering genetic ancestry testing involving mtDNA – a multi-million dollar global industry.*

## 5. Sources to corroborate the impact

- Testimonial from Consultant Scientist on 'Meet the Izzards' and Chief Scientific Officer for BritainsDNA (available from HEI) (confirming importance of research to programme and to genetic ancestry testing industry, and confirming viewing figures for Meet the Izzards)
- The Guardian, 21 February 2013 (link) (re Meet the Izzards viewing figures)
- BBC 2 Programmes, The Incredible Human Journey, Out of Africa (link)